REMARKS

Claims 1-7, 9-23, 26-27, and 38-39 are pending in the application. Claims 2 and 17 have been cancelled, claims 1, 5, 17 and 20 have been amended and new claims 38-39 have been added. Support for the amendment to claim 1 can be found in, *e.g.*, original claim 2. Support for the amendment to claim 16 can be found in, *e.g.*, original claim 17. Support for new claims 38 and 39 can be found in the specification at, *e.g.*, page 4, lines 3-20; page 19, lines 12-23; and original claims 1 and 16. No new matter is added.

Claim Rejections

35 U.S.C. § 112, second paragraph

Claims 4, 6, 19 and 21 have been rejected under 35 U.S.C. § 112, second paragraph as indefinite. According to the Examiner, "it cannot be determined if the limitations in parentheses are a part of the claims and if so, what the limitations are in reference to or if the limitations are a separate entity." (Office action, page 2).

Applicants traverse this rejection. Applicants assert that pending claims 4, 6, 19 and 21 recite specific alleles from the IL-1 gene cluster that contain known polymorphisms the loci of which are represented in the parenthetical number. The recited IL-1 gene cluster alleles are genotypic markers and generally have single nucleotide polymorphisms or nucleotide repeats at a given position in the gene, which is provided in the parentheses. (See, Specification at, *e.g.*, page 12, line 17 to page 13, line 19; page 15, line 21 to page 16, line 2; page 17, lines 7-21.) The specification describes polymorphisms of specific alleles of IL-1 gene family members at, *e.g.*, page 12, line 17 to page 13, line 19. The specification further discloses polymorphisms within the TNF alpha gene. For example, the term "allele 2 of TNFA (-308)" describes a given allele of the TNF alpha gene having a specific polymorphism at position -308 of the gene; the "-" sign indicates that the locus is upstream of the termination start site, while a "+" sign indicates that a locus is downstream of the transcription start site. The specification discloses that the TNFA (-308) polymorphism is a biallelic polymorphism involving the substitution of guanine (G) by adenosine (A) in the less common (TNF2) allele 2. (See, Specification at page 15, lines 21-24; and Wilson et al. (1992) Hum Mol Genet 1:353)). Further, the specification discloses methods

by which one skilled in the art can distinguish the various allelic polymorphisms. (See, *e.g.*, Example 5.1 "*Genotyping subjects.*") Moreover, the alleles recited in pending claims 4, 6, 19 and 21 are presented in an art-recognized manner such that one of skill in the art would recognize their meaning (See, *e.g.*, U.S. Patents 6,210,872, 6,140,047, 5,698,399 and 5,686,246; Kornman et al. (1997) J. Clin Periodontol 24: 72-77; and Clay et al., (1996) Hum Genet 97:723-26.) Therefore, Applicants assert that the recitation of the specific gene locus contained in the parenthetical number allows one to determine to what limitation in the claim the parenthetical number is in reference.

Thus, Applicants assert that claims 4, 6, 19 and 21 are definite, and this rejection should be withdrawn.

35 U.S.C. § 102

Claims 1, 2, 5, 7, 16, 17, 20, 22, 23 and 26 have been rejected as being anticipated by Potter, US Patent number 5,780,587 ("Potter"). Claims 2 and 17 have been cancelled herein. Thus, this rejection is moot in respect to these claims. The Examiner states that Potter teaches a method for identifying a substance that is likely to prevent or diminish a specific biological response in a subject having an inflammatory disease-associated genotype, citing numerous passages from Potter. (Office action, pages 2-3). Applicants traverse the rejection to the extent it applies to claims 1, 5, 7, 16, 20, 22, 23 and 26, as amended herein, for the following reasons.

Potter does not teach one of skill in the art how to identify a test subject having an inflammatory disease-associated genotype, as required by the current claims. Further, there are no teachings in Potter that Alzheimer's disease is an inflammatory disease. Moreover, Applicant asserts that Potter does not teach that a biomarker is observed in a test subject having an inflammatory disease-associated genotype, as required by the pending claims. Potter teaches in the Background section that linkage analysis in two groups suggests lesions in chromosome 21 contribute to some cases of Alzheimer's disease. (See, Potter, col. 2, lines 18-46). Potter also teaches that the ApoE3 isoform of apolipoprotein E3 "is associated with a much later age of onset of familial Alzheimer's disease." (See, Potter, col. 6, lines 7-9). Still, there is no teaching in Potter regarding the use of a test subject having an inflammatory disease-associated genotype.

Thus, Applicants assert that Potter cannot anticipate the present invention. However, in order to advance prosecution, claim 1 has been amended herein to incorporate the subject matter of claim 2; specifically, that the test subject has at least one inflammatory disease-associated allele selected from the group consisting of an IL-1A allele, an IL-1B allele, an IL-1RN allele, a TNF-A allele and an IL-13 allele. Claim 16 has been similarly amended to incorporate the subject matter of claim 17. As previously, stated, Applicants assert that Potter does not teach use of a test subject having an inflammatory disease-associated genotype. In the Office action, the Examiner stated at page 3 that, in regard to claims 2 and 17, "Potter et al. teach the embodiments of claims [2] and 17, wherein said subject has at least one inflammatory disease associated with an IL-1 receptor." While Applicants do not necessarily agree with the Examiner's position regarding Potter's teaching of an "association" between Alzheimer's disease and an IL-1 receptor, Applicants respectfully assert that any such association is irrelevant. Applicants assert that Potter does not teach any allele that is correlated with the occurrence of Alzheimer's disease or the severity of Alzheimer's disease, much less an allele of a gene encoding an IL-1 receptor, or any of the specific inflammatory disease-associated alleles recited in amended claims 1 and 16 (*i.e.*, an IL-1A allele, an IL-1B allele, an IL-1RN allele, a TNF-A allele or an IL-13 allele). The specification defines an "inflammatory disease-associated genotype" or "inflammatory genotype" as "a genotype including one or more alleles that are correlated with the occurrence of a particular inflammatory disease or some aspect (such as severity) of an inflammatory disease." (See, Specification, page 9, lines 26-29.)

Thus, because Potter does not teach the limitation of claims 1 and 16 that the subject has at least one inflammatory disease-associated allele (which can be an IL-1A allele, an IL-1B allele, an IL-1RN allele, a TNF-A allele or an IL-13 allele), this reference does not teach all the limitations of amended claims 1 and 16.

The remaining claims, claims 5, 7, 20, 22, 23 and 26, depend, directly or indirectly, on claims 1 and 16, and, thus, contain all the limitations of claim 1 and 16. Therefore, these claims are also not anticipated by Potter.

For the above-stated reasons, Applicants assert that claims 1, 5, 7, 16, 20, 22, 23 and 26, as amended herein, are not anticipated by Potter, and request withdrawal of this rejection.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance, and a Notice of Allowance is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Ivor R. Elrifi, Reg. No. 39,529
Naomi S. Biswas, Reg. No. 38,384
Cynthia A. Kozakiewicz, Reg. No. 42,764
Attorneys for the Applicant
c/o MINTZ, LEVIN
Please address all correspondence to
customer number **30623**
Tel: (617) 542-6000
Fax: (617) 542-2241

Dated: June 1, 2005

TRA 1994392v1